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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/631,351

Filing Date: July 31, 2003

Appellant(s): HARNACK ET AL.

Mr. Bradley Lytle
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 8 May 2008 appealing from the Office action mailed 8 August 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

2003/0027195	FORD et al.	2-2003
5,516,703	CALDWELL et al.	5-1996
2002/0050220	SCHUELLER et al.	5-2002
4,649,071	TAJIMA et al.	3-1987

Klein et al. "Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines", Applied Physics Letters, Vol. 78, no. 16 (April 16, 2001). pgs. 2396-2398.

Berning et al. "198-Au-Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals" 1998, Nuclear Medicine & Biology, Vol. 25, pages 577-583.

Fan et al. "Adsorption of Surface-Modified Colloidal Gold Particles onto Self-Assembled Monolayers: A Model System for the Study of Interactions of Colloidal Particles and Organic Surfaces", Langmuir, 1997, Vol. 13, pages 119-121.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
1. Claims 2-11, 14-18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Klein et al. (Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines, 2001, Applied Physics, vol. 78, pgs. 2396-2398).

Regarding claims 2, 3 and 14-18 Ford et al. teach a method of attaching a hydrophilic species to hydrophilic macromolecules immobilized on a surface, comprising the steps: providing a surface (par. 0019; par. 0078; par. 0082); immobilizing hydrophilic nucleic acids (hydrophilic macromolecules) on the surface (par. 0019; par. 0078; par. 0082); and exposing the nucleic acids immobilized on the surface to metal complexes

(par. 0079) of gold nanoparticles (a hydrophilic species, par. 0010), whereby the hydrophilic species are attached to the hydrophilic macromolecules (metallization of DNA shows metal particle attachment of DNA, par. 0079), and wherein the nucleic acid is DNA (par. 0020) and is double-stranded or single-stranded (par. 0020). Ford et al. fail to teach the surface being hydrophobic.

Klein et al. teach a hydrophobic substrate (polystyrene coated silicon, pg. 2396, right column, second paragraph) having a nucleic acid immobilized directly to the polystyrene surface (one end of the DNA binds to polystyrene, pg. 2396, right column, second paragraph), in order to provide an attachment method that is highly parallel.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al., attachment of one end of nucleic acids on a hydrophobic surface as taught by Klein et al., in order to provide an attachment method that is easy to employ and results in high yield.

With respect to claims 4 and 11, Ford et al. teach the hydrophilic species in a water solution (par. 0023).

Regarding claims 5, 6 and 20, Ford et al. teach an additional step of growing an attached hydrophilic species to a larger size and wherein the attached hydrophilic species is exposed to an electroless plating solution (enlargement of particles by electroless deposition, par. 0010). Ford et al. further teach the electroless plating solution (par. 0011; par. 0030) comprising a gold salt and a reducing agent (solution contains metal ion species of Au and reducing reagent, par. 0011).

With respect to claims 7-10, Klein et al. teach immobilizing the hydrophilic macromolecules on the surface by applying the hydrophilic macromolecules to the surface by dip-coating (pg. 2396, right column, second paragraph). Ford et al. teach exposing the hydrophilic macromolecules to the species for 10 minutes (par. 0079), which is encompassed by the recited ranges of between 1 second and 20 minutes and between 10 seconds and 10 minutes. Wherein the surface is hydrophobic as taught by Klein et al.

2. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Klein et al. (Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines, 2001, Applied Physics, vol. 78, pgs. 2396-2398) in light of Tajima et al. (US 4,649,071).

Ford et al. in view of Klein et al. teach a hydrophobic substrate being polystyrene, but fail to teach the specific water contact angle properties of polystyrene. However, Tajima et al. teach that an untreated polystyrene surface has water contact angle of 85° (example 5), which is encompassed by the recited ranges of from 30° to 110° and 60° to 110°.

3. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Klein et al. (Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines, 2001, Applied Physics, vol. 78, pgs. 2396-2398), as applied to claim 2, further in view of Berning et al.

(¹⁹⁸Au-Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals, 1998, Nuclear Medicine & Biology, Vol. 25, pages 577-583).

Ford et al. in view of Klein et al. teach a method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, but fail to teach the hydrophilic species being tris(hydroxymethyl)phosphine-gold nanoparticles.

Berning et al. teach a hydrophilic species of tris(hydroxymethyl)phosphine-gold nanoparticles (581, Discussion, 1st paragraph), in order to evaluate their potential utility in the design of Au(I)-containing drugs.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al. in view of Klein et al., a tris(hydroxymethyl)phosphine-gold nanoparticle as taught by Berning et al., in order to provide metal complexes that exhibit *in vitro* stability.

4. Claims 2-11, 14-16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Schueller et al. (US 2002/0050220).

Regarding claims 2, 3 and 14-18 Ford et al. teach a method of attaching a hydrophilic species to hydrophilic macromolecules immobilized on a surface, comprising the steps: providing a surface (par. 0019; par. 0078; par. 0082); immobilizing hydrophilic nucleic acids (hydrophilic macromolecules) on the surface (par. 0019; par. 0078; par. 0082); and exposing the nucleic acids immobilized on the surface to metal complexes (par. 0079) of gold nanoparticles (a hydrophilic species, par. 0010), whereby the

hydrophilic species are attached to the hydrophilic macromolecules (metallization of DNA shows metal particle attachment of DNA, par. 0079), and wherein the nucleic acid is DNA (par. 0020) and is double-stranded or single-stranded (par. 0020). Ford et al. fail to teach the surface being hydrophobic.

Schueller et al. teach a hydrophobic substrate (polystyrene, par. 68) having a biological molecule immobilized directly to the polystyrene surface (biological molecules stamped directly onto a polystyrene surface, par. 68; biological molecule may be a protein or nucleic acid, par. 68), in order to provide an improved method for stamping materials on a substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al., nucleic acids directly onto a hydrophobic surface as taught by Schueller et al., in order to provide a method for attachment of molecules that is more efficiently processed.

With respect to claims 4 and 11, Ford et al. teach the hydrophilic species in a water solution (par. 0023).

Regarding claims 5, 6 and 20, Ford et al. teach an additional step of growing an attached hydrophilic species to a larger size and wherein the attached hydrophilic species is exposed to an electroless plating solution (enlargement of particles by electroless deposition, par. 0010). Ford et al. further teach the electroless plating solution (par. 0011; par. 0030) comprising a gold salt and a reducing agent (solution contains metal ion species of Au and reducing reagent, par. 0011).

With respect to claims 7-10, Ford et al. teach immobilizing the hydrophilic macromolecules on the surface by applying the hydrophilic macromolecules to the surface (par. 0078) by spin-coating (par. 0078). Ford et al. further teach exposing the hydrophilic macromolecules to the species for 10 minutes (par. 0079), which is encompassed by the recited ranges of between 1 second and 20 minutes and between 10 seconds and 10 minutes. Wherein the surface is hydrophobic as taught by Schueller et al.

5. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Schueller et al. (US 2002/0050220) in light of Tajima et al. (US 4,649,071).

Ford et al. in view of Schueller et al. teach a hydrophobic substrate being polystyrene, but fail to teach the specific water contact angle properties of polystyrene. However, Tajima et al. teach that an untreated polystyrene surface has water contact angle of 85° (example 5), which is encompassed by the recited ranges of from 30° to 110° and 60° to 110°.

6. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ford et al. (US 2002/0065242) in view of Schueller et al. (US 2002/0050220), as applied to claim 2, further in view of Berning et al. (¹⁹⁸Au-Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals, 1998, Nuclear Medicine & Biology, Vol. 25, pages 577-583).

Ford et al. in view of Schueller et al. teach a method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, but fail to teach the hydrophilic species being tris(hydroxymethyl)phosphine-gold nanoparticles.

Berning et al. teach a hydrophilic species of tris(hydroxymethyl)phosphine-gold nanoparticles (581, Discussion, 1st paragraph), in order to evaluate their potential utility in the design of Au(I)-containing drugs.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Ford et al. in view of Schueller et al., a tris(hydroxymethyl)phosphine-gold nanoparticle as taught by Berning et al., in order to provide metal complexes that exhibit *in vitro* stability.

(10) Response to Argument

7. At pages 6-7, Appellant argues that it is undisputed that neither Ford nor Klein discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species because one of ordinary skill in the art would have no reason to expect that the method of Ford would function employing a hydrophobic substrate as disclosed in Klein. Appellant argues that Caldwell et al. teach that hydrophilic species of water soluble globular proteins or antibodies absorb irreversibly and non-specifically to hydrophobic surfaces so one having ordinary skill would not expect to be able to control the deposit of hydrophilic species on a hydrophobic substrate which would have dissuaded one in

the art from attempting to replace the hydrophilic substrate of Ford with the hydrophobic substrate of Klein.

8. Appellant's argument is not persuasive because Caldwell et al. focus on the disadvantages of binding a hydrophilic species of antibodies and proteins directly to a hydrophobic substrate. In the combination of Ford and Klein, the hydrophilic species is a gold nanoparticle and binds to a hydrophilic macromolecule on a substrate. Caldwell et al. teach a hydrophilic species of an antibody or protein bound directly to a hydrophobic substrate. This comparison is improper because the "species" of Ford/Klein (nanoparticles) and Caldwell et al. (antibody/protein) are completely different types of species. The comparison is further improper because the proteins of Caldwell bind directly to the substrate, and the hydrophilic species of Ford/Klein bind to hydrophilic macromolecules on the substrate. Therefore, the teachings of Caldwell et al. are not relevant to the current rejections and do not teach that the nanoparticles of Ford would become non-specifically bound to a hydrophobic substrate of Klein. Furthermore, as taught by Klein et al. one end of a hydrophilic macromolecule, DNA, binds preferentially to a hydrophobic substrate. Ford et al. teach one end of a hydrophilic macromolecule, DNA, binding to a hydrophilic substrate and a hydrophilic species binding to the hydrophilic macromolecule. Therefore, for the advantages stated in the rejection above, it would have been advantageous to bind the hydrophilic macromolecules (DNA) to a hydrophobic substrate as taught by Klein et al. instead of a hydrophilic substrate as taught by Ford et al. and one having ordinary skill in the art would have a reasonable expectation of success. Additionally, since the hydrophilic

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species (nanoparticles) of Ford et al. bind almost exclusively to the immobilized nucleic acid, one having ordinary skill in the art would have had further reasonable expectation of success of binding the nanoparticles to the DNA with a hydrophilic or hydrophobic substrate.

9. At page 7, appellant argues that Fan describes adsorption of gold nanoparticles to self-assembled monolayers having differing degrees of hydrophobicity and a greater adsorption of gold particles is present for a more hydrophobic surface which confirms that colloids adsorb from an aqueous solution more extensively to a hydrophobic surface and therefore one having ordinary skill in the art would not expect to control the deposit of hydrophilic species on a hydrophobic substrate. However appellant's argument is not persuasive because Fan et al. teach that a hydrophilic nanospecies will adsorb to a hydrophilic or hydrophobic substrate. Since adsorption of a nanospecies to a substrate occurs whether the substrate is hydrophilic or hydrophobic, one having ordinary skill would not be dissuaded from using a hydrophobic or hydrophilic substrate based only on the amount of adsorption since adsorption occurs with both substrates. Furthermore, the claims do not exclude adsorption of gold particles to the substrate.

10. At page 8, appellant additionally argues that Klein does not suggest employing hydrophobic substrates because Klein discloses that patterned DNA on a substrate can serve as a template for wires, but is taught in the context of hydrophilic substrates. Appellant's argument is not persuasive because Klein is not relied upon for the teaching of wire templates wherein hydrophilic substrates are used, but is instead relied upon for the teaching of DNA immobilized to hydrophobic substrates.

11. At page 8, appellant argues that the discovery of exposure of a hydrophilic species to a hydrophobic substrate on which the hydrophilic macromolecules are immobilized provides a desirable, unexpected result and that the hydrophilic species binds almost exclusively to the hydrophilic molecule and does not bind non-specifically to the hydrophobic substrate as would have been expected in view of past experience relating to the binding of hydrophilic species to hydrophobic substrates. Appellant's argument is not persuasive because Ford et al. teach a hydrophilic macromolecule bound to a hydrophilic substrate with a hydrophilic species bound to the hydrophilic macromolecule. Klein et al. teach an advantage of binding the same type of hydrophilic macromolecule (DNA) directly to a hydrophobic substrate. One having ordinary skill would have expected a reasonable expectation of success of binding the DNA hydrophilic macromolecule to a hydrophobic substrate instead of a hydrophilic substrate as evidenced by Klein et al.

12. At pages 9-10, appellant argues that Tajima et al. and Berning et al. fail to teach immobilization of a hydrophilic macromolecule on a hydrophobic substrate and exposing the macromolecules to a hydrophilic species. Appellant's argument is not persuasive because Tajima and Berning are not relied upon for teaching the entire method in its entirety.

13. At pages 10-11, appellant argues that one having ordinary skill in the art would not have expected that the method of Ford would function employing a hydrophobic substrate as disclosed in Schueller for the reasons discussed above with respect to Ford and Klein. Appellant's argument is not persuasive for the reasons stated above

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with respect to the arguments against Ford and Klein. Appellant further argues that Schueller discloses both a hydrophobic substrate and a hydrophilic substrate, which is not a suggestion that hydrophobic substrate may be employed because of the difficulties related to non-specific adsorption to hydrophobic substrates. Appellant's argument is not persuasive because according to Schueller the hydrophilic macromolecules will bind directly to the hydrophobic substrate. Ford et al. teach that the hydrophilic species will bind to the hydrophilic macromolecule and does not teach away from a hydrophobic substrate. Therefore it would have been obvious to use a hydrophobic substrate as described by Schueller et al. for a more efficient attachment of molecules to a substrate.

14. Appellant also argues that neither Ford nor Schueller discloses or suggests combining immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Appellant's argument is not persuasive because the rejection is made under 35 USC 103(a) and therefore each reference does is not relied upon for teaching the method in its entirety.

15. At pages 12-13, appellant argues that Tajima and Berning fail to teach immobilization of a hydrophilic macromolecule on a hydrophobic substrate and exposing the macromolecules to a hydrophilic species. Appellant's argument is not persuasive because Tajima and Berning are not relied upon for the recited method in its entirety.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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